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14. ABSTRACT This research project will build upon the Long Island Breast Cancer Study Project (LIBCSP), a large population-based, case-control study of the environment and breast cancer. Participants completed an in-person interviewer-administered interview, donated blood and urine samples and had home environment samples (dust, soil and water) collected. For this study, 200 cases and 200 controls who donated urine samples will be selected and their urine samples will be analyzed for a panel of EE biomarkers. In addition, these same women will be screened for polymorphisms in both the estrogen receptor alpha and beta genes. Breast cancer risk in relation to the combination of these multiple EE exposures and gene-environment interaction will be investigated using sophisticated statistical methods such as hierarchical regression models and factor analysis. Additionally, a pilot investigation of the correlation between EE levels in house dust and urinary biomarker levels will be conducted. Currently, samples for this study have been selected and the laboratory analyses are underway. Results of the proposed research project will be of enormous public health relevance since they may advance our knowledge of modifiable breast cancer risk factors and newly identified EEs, thereby providing information that is essential for primary prevention.

15. SUBJECT TERMS
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Introduction

The primary aim of the multidisciplinary postdoctoral award is to position Dr. Teitelbaum as an independent research scientist specializing in the environmental and molecular epidemiology of combined effects of multiple exposures. The research aims – relating multiple environmental estrogen exposure to breast cancer risk – will be examined in the Long Island Breast Cancer Study Project, a large population-based case-control study of breast cancer and the environment.

Specific Aims:

- To investigate whether women with higher combined exposure levels to multiple environmental estrogens are at increased risk of breast cancer.
- To investigate the possibility that women who carry adverse alleles in the estrogen receptor alpha and beta genes and have higher combined exposure levels to multiple environmental estrogens are at higher risk of breast cancer than women without these alleles.
- To evaluate the relationship between household dust and urinary levels of environmental estrogens.

Body

Below I have detailed the training and research that has been completed over the past year according to the tasks outlined in the Statement of Work.

Task 1. To undertake the proposed training program:

a. Complete graduate coursework in biostatistics, genetics, and pharmacology

• Completed three courses in advanced statistical methods: Structural Equation Methods; Applied Longitudinal Analysis; and Mixed Models Analyses Using the SAS System.

• Completed short tutorial for conducting haplotype case-control data analysis: Statistical Analysis of Haplotype-Disease Associations using HAPSTAT.

b. Conduct several epidemiologic analyses of multiple environmental exposures

• Author and co-author on multiple publications (see Reportable Outcomes)

• Continue to participate in departmental environmental and biometry journal clubs, attend monthly meetings of departmental projects, attend weekly Cancer Center seminars and Mount Sinai grand rounds on endocrinology, breast pathology, and oncology.

• Attended and presented at the departmental biometry and environmental epidemiology journal clubs.

• Attended monthly meeting of the NIEHS Center for Children's Environmental Health

• Attended Cancer Center seminars and grand rounds when topics were relevant to my research and training goals

c. Become a member of and alternately attend annual meetings of the International Society of Exposure Analysis (ISEA)/International Society for Environmental Epidemiology (ISEE) and Eastern North American Region of the International Biometric Society (ENAR).

• Current member of:

- International Society for Environmental Epidemiology
- Eastern North American Region of the International Biometric Society
- American Association for Cancer Research (AACR) and Molecular Epidemiology Working Group of AACR
- Society for Epidemiologic Research

• Attended professional scientific meetings:

- International Society of Environmental Epidemiology (ISEE) and presented a poster on “How Representative is a Single Urine Sample of a Six-Month Average for Urinary Phthalate Metabolites and Bisphenol A?”
- Emerging Topics in Breast Cancer and the Environment
- Eastern North American Region of the International Biometric Society (ENAR)
- Cornell University’s Breast Cancer and Environment Research Factors Forum

d. Complete an internship in the lab conducting genetic screening to gain an appreciation for laboratory work commonly performed in molecular epidemiology studies.

• Completed in year 2.

e. Regularly meet with my mentors and advisors to oversee my progress and research development.

• Met both formally and informally with Dr. Wolff each week to review progress, discuss issues related to conducting research and professional development.

• Met with other mentors and advisors on an "as needed" basis depending on the specific research issue requiring discussion

Task 2. To conduct a case-control study of combined environmental estrogen exposure, the estrogen receptor alpha and estrogen receptor beta genes and breast cancer:

a. Conduct sample selection for urinary biomarkers (200 cases and 200 controls) and dust analysis (50 cases and 50 controls)

• Competed.

b. Conduct urinary biomarker environmental estrogen assays.

• Several in-person meetings, phone conferences and email communication with collaborators from the CDC (where biomarker assays will be conducted) have been held.

• Delays in obtaining CDC IRB approval (now approved) and the extensive backlog for performing urinary biomarker analyses have created delays in these analyses. The LIBCSP urine samples are now in the queue at the CDC. The head of the lab estimates that results from the analysis of the samples from this study will not be available for another year. Communication with the CDC lab will continue throughout this period to monitor their progress.

c. Conduct screening for estrogen receptor alpha and estrogen receptor beta genetic polymorphisms.

• The availability of new genotype screening methodology (SNPlex) provided through the Mount Sinai DNA Core delayed the screening of DNA samples. In consultation with Drs. Wetmur and Chen, it was decided that a haplotype approach to examining the association between estrogen receptor genes and breast cancer would be superior to the single SNP approach that was originally proposed. The set of haplotype tagging SNPs has been identified and the DNA samples will be transferred to the DNA core for analysis. Results will be available in the next few months.

d. Conduct house dust environmental estrogen analyses.

• All selected dust samples were located in repository freezers.

• A backlog of work at the laboratory created delays in processing/analyses of the dust samples. The laboratory has completed the analysis of 30 samples – the data indicates that phenolic compounds are measurable in the dust samples that had been frozen for almost 10 years. The laboratory is continuing to work on the remaining 70 samples and estimates that the analysis results will be available in approximately one year.

e. Conduct quality control and verification of data.

• Due to the delay in data, quality control and verification of the data will occur when the data becomes available.

• Review of the data delivered on the first 30 dust samples verified that phenolic compounds were present in the household dust samples selected from the Long Island Breast Cancer Study Project study participants.

Task 3. To conduct data analysis, manuscript preparation and dissemination of research results at conferences

• As laboratory results become available this task will begin.

Key Research Accomplishments

• Designed and oversaw field operations of a methodological study to assess the inter- and intra-person variability of urinary metabolites of the environmental estrogens, including bisphenol A, phthalates and pyrethroid pesticides.

- The collection of serial urine samples was completed.

- The CDC has competed sample analysis and has delivered the biomarker analyte results.
- Using this data, two abstracts have been presented at the Annual meeting of the International Society of Environmental Epidemiology.
- The first of manuscript based on this data is under review at Environmental Research and two more manuscripts are in preparation.

• Published manuscript examining combined effect of multiple exposures "Reported residential pesticide use and breast cancer risk on Long Island, New York" 2007 American Journal of Epidemiology.

Reportable Outcomes

• Publications

Teitelbaum SL, Gammon MD, Britton JA, Neugut AI, Levin B, Stellman SD. Reported residential pesticide use and breast cancer risk on Long Island, NY. Reported residential pesticide use and breast cancer risk on Long Island, New York. Am J Epidemiol. 2007 Mar 15;165(6):643-51.

Wolff MS, Teitelbaum SL, Windham G, Pinney SM, Britton JA, Chelimo C, Godbold J, Biro F, Kushi LH, Pfeiffer CM, Calafat AM. Pilot study of urinary biomarkers of phytoestrogens, phthalates, and phenols in girls. Environ Health Perspect. 2007 Jan;115(1):116-21.

Teitelbaum, SL, Calafat, AM, Britton, JA, Silva, MJ, Ye, X, Kuklenyik, Z, Reidy, JA, Brenner, BL, Galvez, MP, Wolff, MS. Temporal variability in urinary phthalate metabolites, phenols and phytoestrogens among children. (Under review: Environmental Research)

Teitelbaum, SL, Calafat, AM, Britton, JA, Silva, MJ, Ye, X, Kuklenyik, Z, Reidy, JA, Brenner, BL, Galvez, MP, Wolff, MS. Urinary phthalate metabolite concentrations and reported use of personal care products. (abstract accepted for International Society of Environmental Epidemiology 2007)

Teitelbaum, SL, Calafat, AM, Britton, JA, Silva, MJ, Ye, X, Kuklenyik, Z, Reidy, JA, Brenner, BL, Galvez, MP, Wolff, MS. How Representative is a Single Urine Sample of a Six-Month Average for Urinary Phthalate Metabolites and Bisphenol A? Epidemiology. 17(6) Suppl:S335-S336, 2006.

Windham G, Wolff M, Pinney S, Teitelbaum S, Calafat A, Sjodin A, Pfeiffer C, Barr D, Erdmann C, Koblick K, Collmann G. Biomarkers of Environmental Exposures in a Multi-Site Study of Young Girls. Epidemiology. 17(6) Suppl:S419, 2006.

Teitelbaum SL, Gammon MD, Britton JA, Neugut AI, Levin B, Stellman SD, Wolff MS. Characteristics and patterns of residential pesticide use on Long Island, NY. (submitted to Environmental Health Perspectives)

Teitelbaum SL, et al. Environmental chemicals in household dust and breast cancer risk on Long Island, NY. (in preparation)

Teitelbaum SL, et al. The combined effect of multiple environmental exposures on pregnancy outcome in the World Trade Center Pregnancy cohort. (in preparation)

Teitelbaum SL, et al. Interaction of PCB exposure with Cyp1A1 genetic polymorphisms and breast cancer risk on Long Island, NY. (in preparation)

• Principal Investigator of NIEHS funded Mentored Scientist Career Development Award.
• Co-Investigator on Project 2 of NIEHS/EPA funded "Breast Cancer and the Environment Research Center" (MS Wolff, PI).
• New investigator award in our department's NIEHS/EPA funded Children's Environmental Health Center.
• Abstract reviewer for 3rd annual Breast Cancer and the Environment Research Symposia.
• Planning committee member for 4th annual Breast Cancer and the Environment Research Symposia.
• Peer reviewer for several prominent journals in epidemiology and environmental research
• Selected as a member of NIEHS study section for SuperFund Projects
• Invited for Board Membership of "The Open Epidemiology Journal"

Conclusions

I have made significant progress towards becoming an independent research scientist specializing in the environmental and molecular epidemiology of combined effects of multiple exposures. I have extended my multiple exposure study opportunities by obtaining 2 additional federally funded initiatives and increased my

ability to conduct multiple exposure epidemiologic analyses through the training I have completed. The work accomplished during the third year of this grant has built a strong foundation for completing the proposed research in the additional year of this project provided by the no-cost extension of this award. The research I have conducted thus far is directly related to the goals of my postdoctoral award. All of these urinary metabolites measured in the temporal variability study will be measured in the urine samples of the case-control study analyses that will be completed in the coming year of this award. The results provide invaluable information for the data analysis of the case-control study and contribute to our understanding of how these biomarkers can be best used in future epidemiologic studies.

References

None

Appendices

None